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=> d his full

     (FILE 'HOME' ENTERED AT 15:00:09 ON 17 JUN 2002)

     FILE 'CAPLUS' ENTERED AT 15:00:18 ON 17 JUN 2002
L1            57 SEA ABB=ON  PLU=ON  DROSPIRENONE
L2             2 SEA ABB=ON  PLU=ON  DROSPIRENONE (P) (MICROPARTICLES OR
                 MICRONIZ? OR MICROSPHERES OR PARTICLES)
                 D L2 IBIB KWIC
                 D L2 IBIB KWIC 1-
L3            36 SEA ABB=ON  PLU=ON  PROGESTIN (P) (MICROPARTICLES OR MICRONIZ?
                 OR MICROSPHERES OR PARTICLES)
L4            30 SEA ABB=ON  PLU=ON  PROGESTIN (P) (MICROPARTICLES OR MICRONIZ?
                 OR MICROSPHERES OR PARTICLES) (P) (ESTROGEN OR ESTRADIOL)
L5             3 SEA ABB=ON  PLU=ON  PROGESTIN (5A) (MICROPARTICLES OR MICRONIZ?
                  OR MICROSPHERES OR PARTICLES) (P) (ESTROGEN OR ESTRADIOL)
                 D L5 IBIB KWIC 1-
L6             0 SEA ABB=ON  PLU=ON  L4 AND DROSPIRENONE
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=> d l4 ibib kwic 10-30

L4 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:261249 CAPLUS
DOCUMENT NUMBER: 133:26919
TITLE: Preserving cardiovascular benefits of hormone replacement therapy
AUTHOR(S): Bush, Trudy L.
CORPORATE SOURCE: Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, 21201, USA
SOURCE: Journal of Reproductive Medicine (2000), 45(3, Suppl.), 259-272
CODEN: JRPMAP; ISSN: 0024-7758
PUBLISHER: Journal of Reproductive Medicine, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review, with 36 refs. In the premenopausal period, the risk of heart disease is considerably lower in women than in men; however, in the postmenopausal period, when **estrogen** levels are considerably lower, women's risk of heart disease increases dramatically and approaches that of men. Numerous animal studies, using a variety of models, also confirm **estrogen**'s cardioprotective effect. Although the results of numerous population-based, observational studies have demonstrated a lower risk of heart disease in women who receive **estrogen** replacement therapy, evidence from prospective, randomized clin. trials is scant. The Postmenopausal **Estrogen/Progestin** Intervention (PEPI) trial evaluated cardiovascular risk factors, not events, in a large, prospective, randomized trial and found that **estrogen** improved lipid profiles and other known risk factors. In addn., the PEPI trial compared several **estrogen**/progestogen treatment regimens, including both medroxyprogesterone acetate (MPA) and **micronized** progesterone (MP), and found that combined hormone replacement therapy regimens including MP attenuated the beneficial effects of **estrogen** less than those contg. MPA. In the Heart and **Estrogen/Progestin** Replacement Study (HERS), however, which prospectively evaluated whether **estrogen** and MPA use reduced the no. of nonfatal myocardial infarctions and cardiovascular events, no effect was seen. Although HERS was a null trial, the vast literature base showing a cardioprotective effect should not be discounted. Further research will be required before blanket recommendations on the cardioprotective effects of hormone therapy can be made.

L4 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:43726 CAPLUS
DOCUMENT NUMBER: 132:103042
TITLE: Impaired procoagulant-anticoagulant balance during hormone replacement therapy? A randomised, placebo-controlled 12-week study
AUTHOR(S): Van Baal, W. Marchien; Emeis, Jef J.; Van der Mooren, Marius J.; Kessel, Hilda; Kenemans, Peter; Stehouwer, Coen D. A.
CORPORATE SOURCE: Institute Cardiovascular Research, Dep. Obstetrics Gynecology, Vrije Univ. Amsterdam, Amsterdam, 1007 MB, Neth.
SOURCE: Thrombosis and Haemostasis (2000), 83(1), 29-34
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: F. K. Schattauer Verlagsgesellschaft mbH
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB In this randomized, placebo-controlled 12-wk study, 60 healthy postmenopausal women received either placebo (N=16) or daily 2 mg **micronized estradiol**, either unopposed (N=16, E2 group) or combined with a progestagen for 14 days of each cycle (N=28, E2 + P group). As compared to placebo, blood plasma levels of AT III were reduced only in the E2 group (.apprx.28%), plasma levels of protein C decreased only in the E2 + P group (.apprx.4%) and plasma levels of protein S decreased in both the E2 and E2 + P group (.apprx.21%). In both the E2 and E2 + P groups, the plasma levels of factor VII (antigen and activity) showed a borderline increase (.apprx.10%), whereas no change was obsd. in active factor VII. Plasma levels of tissue-type plasminogen activator (.apprx.22%), urokinase plasminogen activator (.apprx.25%) and plasminogen activator inhibitor type-1 (.apprx.43%) decreased in the E2 and E2 + P groups, whereas those of plasminogen increased (.apprx.12%). Treatment was assocd. with an increase in levels of prothrombin fragment 1 + 2 (.apprx.31%), but levels of thrombin-antithrombin III complexes, and of plasmin-.alpha.2-antiplasmin complexes and total fibrin(ogen) degrdn. products did not change. Short-term E2 and E2 + P treatment is assocd. with a shift in the procoagulant-anticoagulant balance towards a procoagulant state. A substantial proportion of women do not have a net increase in fibrinolytic activity. These data may be relevant in explaining the increased risk of venous thromboembolism assocd. with ERT and HRT, and possibly also in explaining the neg. results of the Heart and **Estrogen/progestin** Replacement Study.

L4 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:10325 CAPLUS
DOCUMENT NUMBER: 132:260794
TITLE: The effect of hormone replacement therapy on metabolism of lipoprotein remnants in postmenopausal women
AUTHOR(S): Sanada, M.; Nakagawa, H.; Kodama, I.; Sakasita, T.; Ohama, K.
CORPORATE SOURCE: Faculty of Medicine, School of Medicine, Department of Obstetrics and Gynecology, Hiroshima University, Hiroshima, Japan
SOURCE: Maturitas (2000), 34(1), 75-82
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The measurement of remnant-like **particles** reflects chylomicron and very low d. lipoprotein remnants which are most likely atherogenic **particles**. The authors investigated the effects of menopausal status and postmenopausal hormone replacement on metab. of remnant lipoprotein-cholesterol. The authors measured remnant lipoprotein-cholesterol by an immunosepn. assay in 20 premenopausal, 40 postmenopausal, and 30 bilaterally oophorectomized women. Of 70 postmenopausal subjects, 21 surgically menopausal women (with total hysterectomy) were started on hormone replacement with conjugated equine **estrogen**, 0.625 mg/day, and 36 naturally postmenopausal women were begun on a combination of conjugated equine **estrogen** 0.625 mg/day, plus medroxyprogesterone acetate, 2.5 mg/day. Plasma levels of remnant lipoprotein-cholesterol and other common lipids were measured after 6 and 12 mo of treatment. Plasma remnant lipoprotein-cholesterol levels in postmenopausal and surgically menopausal women were significantly higher than in premenopausal women. Plasma total and low-d. lipoprotein cholesterol levels decreased and high-d. lipoprotein cholesterol increased significantly in both treatment groups, resp.

Plasma triglyceride levels were not changed by treatment; however, remnant lipoprotein-cholesterol levels decreased in both treatment groups (**estrogen** group;, **estrogen-progestin** group). No side effects of therapy were consistently reported. The authors confirmed that remnant lipoprotein-cholesterol increases after menopause. Hormone replacement therapy improves disordered lipoprotein metab. and exerts a favorable effect on lipoprotein remnant metab. in postmenopausal women.

L4 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:436254 CAPLUS
DOCUMENT NUMBER: 131:111564
TITLE: Serum and tissue hormone levels of vaginally and orally administered estradiol
AUTHOR(S): Tourgeman, David E.; Gentzchein, Elisabet; Stanczyk, Frank Z.; Paulson, Richard J.
CORPORATE SOURCE: Division of Reproductive Endocrinology and Infertility, Department of, University of Southern California School of Medicine, Los Angeles, CA, 90033, USA
SOURCE: American Journal of Obstetrics and Gynecology (1999), 180(6, Pt. 1), 1480-1483
CODEN: AJOGAH; ISSN: 0002-9378
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB OBJECTIVE: Our purpose was to det. serum and endometrial **estradiol** levels when **micronized estradiol** is administered vaginally and orally. STUDY DESIGN: Five subjects were given oral **estradiol** (2 mg twice daily), during an artificial luteal phase, and another group of 5 subjects were given the same dose of **estradiol** by the vaginal route. Endometrial biopsies and blood samples were obtained on day 21 of the cycle, 2 h after the last dose was administered. Tissue and blood samples were assayed for **estradiol** . RESULTS: Serum **estradiol** levels were significantly higher with vaginally administered **estradiol** than with orally administered **estradiol** (2344.+-.398 vs. 279.+-.76 pg/mL, P <.005). Endometrial **estradiol** concns. were also significantly higher with vaginally administered **estradiol** than with the oral prepn. (918.+-.412 vs. 13.+-.2 pg/mg protein, P <.05). CONCLUSIONS: Vaginal administration of **estradiol** is more effective in increasing serum and endometrial levels of **estradiol** than the oral route and may represent the optimal route of administration for recipients of egg donation. If the vaginal route of **estradiol** administration is considered for menopausal replacement therapy, much lower doses of the std. oral quantities should be used. Furthermore, if the uterus is present, a **progestin** must be used to compensate for the high tissue levels of **estradiol**.

L4 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:329460 CAPLUS
DOCUMENT NUMBER: 131:97712
TITLE: Comparison of the effects of triphasic oral contraceptives with desogestrel or levonorgestrel on apolipoprotein A-I-containing high-density lipoprotein particles
AUTHOR(S): Cheung, Marian C.; Walden, Carolyn E.; Knopp, Robert H.
CORPORATE SOURCE: Northwest Lipid Research Clinic and Laboratories, Division of Endocrinology, Metabolism and Nutrition, Department of Medicine, School of Medicine, University

of Washington, Seattle, WA, 98103, USA
SOURCE: Metabolism, Clinical and Experimental (1999), 48(5), 658-664
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Recent observations suggest that the risk of coronary artery disease (CAD) is assocd. with both the level and compn. of the two major populations of apolipoprotein (apo)-defined high-d. lipoprotein (HDL) **particles** : those contg. both apo A-I and apo A-II [Lp(AI,AII)] and those contg. apo A-I without apo A-II [Lp(AI)]. While sex hormones are known to affect HDL, their influence on these apo-defined HDL **particles** is not known. The authors have detd. the effects of two triphasic oral contraceptive (OC) formulations on these HDL **particles** in healthy normolipidemic women aged 21 to 35 yr. The formulations contain comparable quantities of ethinyl **estradiol** (EE) and either desogestrel (DG), a minimally androgenic **progestin**, or levonorgestrel (LN), a more androgenic **progestin**. Lipid and lipoprotein levels were measured during the third week of the normal menstrual cycle and the sixth month of OC use. The DG/EE formulation significantly increased total cholesterol (C) 15%, triglyceride (TG) 99%, phospholipid (PL) 17%, apo A-I 28%, apo A-II 34%, apo B 21%, very-low-d. lipoprotein cholesterol (VLDL-C) 238%, HDL-C 20%, and HDL3-C 28% (to.005), but not low-d. lipoprotein cholesterol (LDL-C). The LN/EE formulation also increased total C 15%, TG 33%, apo A-I 15%, HDL3-C 21%, apo B 30%, and, addnl., LDL-C 19%. Both formulations increased Lp(AI,AII) (DG/EE, 34%,; LN/EE, 24%). These changes reflected comparable increases of small (7.0 to 8.2 nm) and medium (8.2 to 9.2 nm) **particles** in the LN/EE group and a predominant increase of medium-sized **particles** in the DG/EE group. Also, in the LN/EE group but not the DG/EE group, there were fewer large (9.2 to 11.2 nm) **particles**. Lp(AI) increased only in the DG/EE group (25%) and was due to the presence of more large **particles**. The level of Lp(AI) did not change in the LN/EE group, but the lipid/A-I ratio of these **particles** was lower and there were more small **particles**. Thus, triphasic OC formulations with **progestins** of different androgenicity had different effects on VLDL, LDL, and the level and compn. of HDL **particles** with and without apo A-II, possibly reflecting **estrogen**/**progestin**/androgen balance. **Estrogen** dominance increases both Lp(AI,AII) and Lp(AI) and favors large Lp(AI) **particles**, while **progestin**/androgen dominance increases only Lp(AI,AII) and favors small **particles**. Because of the importance of HDL in the arterial wall physiol., OC formulations with different **estrogen** and **progestin** content may affect arterial wall health to a different extent.

L4 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:174853 CAPLUS
DOCUMENT NUMBER: 130:262341
TITLE: Oral micronized progesterone
AUTHOR(S): De Lignieres, Bruno
CORPORATE SOURCE: Department of Endocrinology and Reproductive Medicine, Hopital Necker, Paris, Fr.
SOURCE: Clinical Therapeutics (1999), 21(1), 41-60
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB This review sought to examine the rationale for selecting an oral **micronized** progesterone formulation rather than a synthetic **progestin** for some of the main indications for progestogens. Unopposed **estrogen** use is assocd. with a high risk (relative risk, 2.1 to 5.7) of endometrial hyperplasia and adenocarcinoma, and it has been understood for some time that a progestogen must be added for at least 10 to 14 days per mo to prevent these effects. However, the most commonly used synthetic **progestins**, norethisterone and medroxyprogesterone acetate, have been assocd. with metabolic and vascular side effects (eg, suppression of the vasodilating effect of **estrogens**) in both exptl. and human controlled studies. All comparative studies to date conclude that the side effects of synthetic **progestins** can be minimized or eliminated through the use of natural progesterone, which is identical to the steroid produced by the corpus luteum. The inconvenience assocd. with the use of injectable, rectal, or vaginal formulations of natural progesterone can be circumvented by using orally administered **micronized** progesterone. The bioavailability of **micronized** progesterone is similar to that of other natural steroids, and interindividual and intraindividual variability of area under the curve is similar to that seen with synthetic **progestins**. A clear dose-ranging effect has been demonstrated, and long-term protection of the endometrium has been established. **Micronized** progesterone has been used widely in Europe since 1980 at dosages ranging from 300 mg/d (taken at bedtime) 10 days a month for women wishing regular monthly bleeding to 200 mg 14 days a month or 100 mg 25 days a month for women willing to remain amenorrheic. This therapy is well tolerated, with the only specific side effect being mild and transient drowsiness, an effect minimized by taking the drug at bedtime. The prospective, comparative Postmenopausal **Estrogens/Progestin** Intervention trial has recommended oral **micronized** progesterone as the first choice for opposing **estrogen** therapy in nonhysterectomized postmenopausal women.

L4 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:173191 CAPLUS
DOCUMENT NUMBER: 130:347559
TITLE: Effects of estrogen and estrogen-progestin on mammographic parenchymal density
AUTHOR(S): Greendale, Gail A.; Reboussin, Beth A.; Sie, Angela; Singh, H. Rosy; Olson, Linda K.; Gatewood, Olga; Bassett, Lawrence W.; Wasilauskas, Carol; Bush, Trudy; Barrett-Connor, Elizabeth
CORPORATE SOURCE: Division of Geriatrics, University of California, Los Angeles, CA, 90095-1687, USA
SOURCE: Annals of Internal Medicine (1999), 130(4, Pt. 1), 262-269
CODEN: AIMEAS; ISSN: 0003-4819
PUBLISHER: American College of Physicians-American Society of Internal Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB In longitudinal studies, greater mammog. d. is assocd. with an increased risk for breast cancer. Studies were carried out to assess differences between placebo, **estrogen**, and three **estrogen-progestin** regimens on change in mammog. d. The design was subset anal. of a 3-yr, multicenter, double-blind, randomized, placebo-controlled trial. Participants consisted of 307 of the 875 women in the Postmenopausal **Estrogen/Progestin** Interventions Trial. Participants had a baseline mammogram and at least one follow-up mammogram available, adhered to treatment, had not taken **estrogen** for at least 5 yr before baseline, and did not have breast implants. Treatments

were placebo, conjugated equine **estrogens** (CEE), CEE plus cyclic medroxyprogesterone acetate (MPA), CEE plus daily MPA, and CEE plus cyclic **micronized** progesterone (MP). Change in radiog. d. (according to American College of Radiol. Breast Imaging Reporting and Data System grades) on mammog. were examd. Almost all increases in mammog. d. occurred within the first year. At 12 mo, the percentage of women with d. grade increases was 0% in the placebo group, 3.5% in the CEE group, 23.5% in the CEE plus cyclic MPA group, 19.4% in the CEE plus daily MPA group, and 16.4% in the CEE plus cyclic MP group. At 12 mo, the odds of an increase in mammog. d. were 13.1 with CEE plus cyclic MPA, 9.0 with CEE plus daily MPA, and 7.2 with CEE plus cyclic **micronized** progesterone compared with CEE alone. Further study of the magnitude and meaning of increased mammog. d. due to use of **estrogen** and **estrogen-progestins** is warranted because mammog. d. may be a marker for risk for breast cancer.

L4 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:806300 CAPLUS
DOCUMENT NUMBER: 130:163339
TITLE: Symptom relief and side effects of postmenopausal hormones: results from the postmenopausal estrogen/progestin interventions trial
AUTHOR(S): Greendale, Gail A.; Reboussin, Beth A.; Hogan, Patricia; Barnabei, Vanessa M.; Shumaker, Sally; Johnson, Susan; Barrett-Connor, Elizabeth
CORPORATE SOURCE: School of Medicine, University of California, Los Angeles, CA, USA
SOURCE: Obstetrics and Gynecology (New York) (1998), 92(6), 982-988
CODEN: OBGNAS; ISSN: 0029-7844
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB To assess pair-wise differences between placebo, **estrogen**, and each of three **estrogen-progestin** regimens on selected symptoms. This was a 3-yr, multicenter, double-blind, placebo-controlled trial in 875 postmenopausal women aged 45-64 yr at baseline. Participants were assigned randomly to one of five groups: 1) placebo, 2) daily conjugated equine **estrogens**, 3) conjugated equine **estrogens** plus cyclical medroxyprogesterone acetate, 4) conjugated equine **estrogens** plus daily medroxyprogesterone acetate, and 5) conjugated equine **estrogens** plus cyclical **micronized** progesterone. Symptoms were self-reported using a checklist at 1 and 3 yr. Factor anal. reduced 52 symptoms to a set of six symptom groups. In intention-to-treat analyses at 1 yr, each active treatment demonstrated a marked, statistically significant, protective effect against vasomotor symptoms compared with placebo (odds ratios [ORs] 0.17-0.28); there was no addnl. benefit of **estrogen-progestin** over **estrogen** alone. Only **progestin**-contg. regimens were significantly assocd. with higher levels of breast discomfort (OR 1.92-2.27). Compared with placebo, women randomized to conjugated equine **estrogens** reported no increase in perceived wt. Those randomized to medroxyprogesterone acetate reported less perceived wt. gain (OR 0.61-0.69) than placebo. Anxiety, cognitive, and affective symptoms did not differ by treatment assignment. Analyses restricted to adherent women were not materially different than those using intention-to-treat, except that women adherent to medroxyprogesterone acetate and **micronized** progesterone regimens reported fewer musculoskeletal symptoms (OR 0.62-0.68). These results confirm the usefulness of postmenopausal hormone therapy for hot flashes, show convincingly that **estrogen** plus **progestin** causes breast discomfort, and demonstrate little

influence of postmenopausal hormones on anxiety, cognition, or affect.

L4 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:235302 CAPLUS
DOCUMENT NUMBER: 128:290380
TITLE: Effect of postmenopausal hormone therapy on lipoprotein(a) concentration
AUTHOR(S): Espeland, Mark A.; Marcovina, Santica M.; Miller, Valery; Wood, Peter D.; Wasilauskas, Carol; Sherwin, Roger; Schrott, Helmut; Bush, Trudy L.
CORPORATE SOURCE: Section on Biostatistics, Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, NC, 27157-1063, USA
SOURCE: Circulation (1998), 97(10), 979-986
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Postmenopausal hormone therapy has been reported to decrease levels of lipoprotein (Lp)(a) in cross-sectional studies and small or short-term longitudinal studies. We report findings from a large, prospective, placebo-controlled clin. trial that allows a broad characterization of these effects for four regimens of hormone therapy. The Postmenopausal **Estrogen/Progestin** Interventions study was a 3-yr, placebo-controlled, randomized clin. trial to assess the effect of hormone regimens on cardiovascular disease risk factors in postmenopausal women 45 to 65 yr of age. The active regimens were conjugated equine **estrogens** therapy at 0.625 mg daily, alone or in combination with each of three regimens of progestational agents: medroxyprogesterone acetate (MPA) at 2.5 mg daily (ie, continuous MPA), MPA at 10 mg days 1 to 12 (ie, cyclical MPA), and **micronized** progesterone at 200 mg days 1 to 12. Plasma levels of Lp(a) were measured at baseline (n=366), 12 mo (n=354), and 36 mo (n=342). Assignment to hormone therapy resulted in a 17% to 23% av. drop in Lp(a) concns. relative to placebo (P<.0001), which was maintained across 3 yr of follow-up. No significant differences were obsd. among the four active arms. Changes in Lp(a) assocd. with hormone therapy were pos. correlated with changes in LDL cholesterol, total cholesterol, apolipoprotein B, and fibrinogen levels and were similar across subgroups defined by age, wt., ethnicity, and prior hormone use. Postmenopausal **estrogen** therapy, with or without concomitant **progestin** regimens, produces consistent and sustained redns. in plasma Lp(a) concns.

L4 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:593911 CAPLUS
DOCUMENT NUMBER: 127:243389
TITLE: The postmenopausal estrogen/progestin interventions study: primary outcomes in adherent women
AUTHOR(S): Barrett-Connor, Elizabeth; Slone, Stacey; Greendale, Gail; Kritz-Silverstein, Donna; Espeland, Mark; Johnson, Susan R.; Waclawiw, Myron; Fineberg, S. Edwin
CORPORATE SOURCE: Department of Family and Preventive Medicine, University of California, La Jolla, CA, 92093-0607, USA
SOURCE: Maturitas (1997), 27(3), 261-274
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Our objective was to assess the efficacy of unopposed **estrogen**, and three **estrogen/progestin** regimens on selected heart disease risk factors among adherent women and to contrast those results with efficacy among all women in the PEPI study. A 3-yr,

multicenter, randomized, double-blinded, placebo-controlled clin. trial. A total of 847 healthy postmenopausal women aged 45 to 64 yr of age with no known contraindication to hormone therapy, who attended their 36 mo clin. visit. Participants were randomized in equal nos. to one of the following treatments: (1) placebo; (2) conjugated equine **estrogen** (CEE) 0.625 mg daily; (3) CEE 0.625 daily plus medroxyprogesterone acetate (MPA) 10 mg, days 1-12; (4) CEE 0.625 daily plus MPA 2.5 mg daily; or (5) CEE 0.625 daily plus **micronized** progesterone (MP) 200 mg, days 1-12. Analyses are based on adherent women, where adherence is defined as taking at least 80% of pills at each 6-mo visit. Adherence rates were high in all groups except women with a uterus assigned to unopposed CEE. The difference in HDL-C levels resulting from the CEE vs. CEE + MP was approx. three times larger than in the intent-to-treat analyses, reaching statistical significance ($P < 0.05$). In each active treatment, LDL-C decreased 10-15%. Triglycerides increased 15-20% in each opposed CEE arm and over 25% in the CEE only arm; this difference was not statistically significant. Fibrinogen increased by 7% among placebo adherers, but decreased or remained fairly stable among the active arm adherers. Systolic blood pressure increased 3-5% in all treatment arms. Women adherent to the CEE + MPA arms had twice the increase of 2 h glucose levels as women adherent to CEE only, or CEE + MP (8-9% vs. 3-4%). Two-hour insulin levels decreased 3-12% for all arms. The patterns of change for fibrinogen, SBP, 2 h glucose and insulin were similar to those from the intent-to-treat analyses. In analyses limited to adherent women, all active treatments, compared to placebo, continued to have similar and favorable effects on LDL-cholesterol and fibrinogen and no significant effects on blood pressure or insulin levels. Given the overall high adherence rates in PEPI, the results are similar to the intent-to-treat analyses, as expected. Only the trend of HDL-C to have a larger increase in the CEE only arm (in the intent-to-treat analyses) gained statistical significance in analyses restricted to adherers.

L4 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:337997 CAPLUS
DOCUMENT NUMBER: 127:964
TITLE: Percutaneous estradiol gel with an intrauterine levonorgestrel releasing device or natural progesterone in hormone replacement therapy
AUTHOR(S): Suvanto-Luukkonen, Eila; Sundstrom, Helena; Penttinen, Jorma; Laara, Esa; Pramila, Sirkka; Kauppila, Antti
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Kainuu Central Hospital, Oulu, 90220, Finland
SOURCE: Maturitas (1997), 26(3), 211-217
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study is to evaluate the bleeding patterns and clin. compliance assocd. with postmenopausal amenorrhea-inducing forms of hormone replacement therapy using either percutaneous **estradiol** -gel and a levonorgestrel-releasing intrauterine device or an oral/vaginal natural progesterone. Sixty postmenopausal women with an intact uterus were followed over 12 mo in this open, non-randomized, parallel group study. All patients continuously received a gel contg. 1.5 mg of **estradiol** daily. The women were divided into three groups on the basis of **progestin** administration. Twenty women (group I) had a levonorgestrel-releasing device (LNG-IUD) inserted at the beginning of the study. Twenty-one women (group II) received oral natural **micronized** progesterone (oral P) 100 mg daily during 25 calendar days each month, and 19 women (group III) used vaginal natural **micronized** progesterone (vaginal P) 100-200 mg daily during 25 calendar days each month (higher dose if spotting occurred). Clinic visits were at 0, 3, 6 and 12 mo. Bleeding patterns were recorded by the

patient in a diary and clin. compliance was evaluated at control visits during the treatment. Symptoms were recorded using a modified Kuppermann index. The serum **estradiol** concn. was detd. at the 0, 6 and 12 mo control visits. 80% (N = 16) of the patients in the LNG-IUD group, 67% (n = 14) in the oral P group II and 53% (n = 10) in the vaginal P group were without bleeding at 12 mo. Spotting was common during the first 3 mo. Symptom relief was good in each group. The LNG-IUD did not cause any serious side-effects. Compliance was good for LNG-IUD and oral progesterone but not for vaginal progesterone. Percutaneous **estradiol**-gel assocd. with LNG-IUD is an appropriate method of hormone replacement therapy. The combination of oral natural progesterone with **estradiol**-gel is also useful, although bleeding episodes complicated the treatment in one third of the patients. The vaginal administration of natural progesterone was impractical due to bleeding disorders.